UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,603	09/17/2003	Guy A. Rouleau	GOUD:023USD1	3929

7590 10/09/2007

Michael R. Krawzsenek
Fulbright & Jaworski L.L.P.
600 Congress Avenue, Suite 2400
Austin, TX 78701

EXAMINER	
LIU, SUE XU	
ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
10/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,603	ROULEAU ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/19/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14 and 34-47* is/are pending in the application.

4a) Of the above claim(s) *35, 42 and 45-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14, 34, 36-41, 43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/27/07;5/2/07;5/30/07;6/22/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-13 and 15-33 have been cancelled.

Claims 34-47 have been added as filed on 3/28/07.

Claims 14 and 34-47 are currently pending.

Claims 35, 42 and 45-47 have been withdrawn;

Claims 14, 34, 36-41, 43 and 44 are being examined in this application.

Election/Restrictions

1. Applicant's election with traverse of Group I (Claims 14-28) in the reply filed on 9/25/06 is as previously acknowledged.

2. Applicant's election with traverse of SEQ ID NO: 65 for the nucleic acid sequence and SEQ ID NO: 67 for the amino acid sequence in the reply filed on 9/25/06 is as previously acknowledged.

3. Applicants have added claims (e.g. Claim 45-47) that recite SEQ ID Nos that were not elected by original presentation.

Newly submitted claims 45-47 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The SEQ ID Nos recited in Claims 45-47 are distinct from SEQ ID No 65 originally elected.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

on the merits. Accordingly, claims 45-47 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. This application contains claims 45-47 drawn to an invention nonelected with traverse in the reply filed on 9/25/06. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

5. Applicant's election with traverse of the following species:

A. Idiopathic Generalized Epilepsy (IGE);

B. flux of ions through the channel;

C. Upon further consideration, this species election is withdrawn;

in the reply filed on 7/19/07 is as previously acknowledged. Accordingly, Claims 35 and 42 are withdrawn due to non-elected species.

Priority

6. This application is a DIVISIONAL of U.S. Patent Application Nos. 09/718,355 (filed 11/24/2000), which claims priority benefit to a US provisional application 60/167,623 (filed 11/26/1999).

Information Disclosure Statement

7. The IDS filed on 4/27/07, 5/2/07, 5/30/07 and 6/22/07 have been considered. See the attached PTO 1449 forms.

Claim Rejections Withdrawn

8. In light of applicants' amendments to the claims, the following claim rejections as set forth in the previous office action are withdrawn:

Claims 14-20, 22, 24, 25, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

10. Claims 14, 34, 36-41, 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection over claims 14-20, 22, 24, 25, 27 and 28 is moot due to

applicant's cancellation of the said claims. The rejection over claims 34, 36-41, 43 and 44 is necessitated by applicant's amendment to the claims.

The instant claims recite a method for selecting a compound which reduces an activity of a SCN3A sodium channel comprising:

(a) contacting a composition comprising a SCN3A sodium ion channel protein with a test compound;

(b) assaying the activity of the sodium ion channel in the presence of the test compound;

(c) comparing the activity of the sodium ion channel in the absence of said test compound;

(d) selecting a compound which reduces the activity of the sodium ion channel as compared to the activity of the sodium ion channel in the absence of the test compound; wherein said SCN3A protein is selected from the group consisting of (i) **an** amino acid sequence set forth in SEQ ID NO:67; and (ii) a SCN3A protein expressed by a SCN3A nucleic acid sequence having at least 95% identity to the nucleic acid sequence as set forth in SEQ ID NO:65.

The instant claim 34 is drawn to method of selecting a compound "capable of reducing voltage-gated ion channel activity of a human SCN3A protein associated with idiopathic generalized epilepsy (IGE)."

To satisfy the written description requirement, applicants may convey reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Applicants may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118.

The written description requirement of 35 U.SC. 112 exists independently of enablement requirement, and the requirement applies whether or not the case involves questions of priority. The requirement applies to all inventions, including chemical inventions, and because the fact that the patent is directed to method entailing use of compound, rather than to compound per se, does not remove patentee's obligation to provide a description of the compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ 2d 1886, 1890-93 (Fed. Cir. 2004).

With regard to the description requirement, applicants' attention is invited to consider the decision of the Court of Appeals for the Federal Circuit, which holds that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it form other materials." University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1405 (1997), quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in University of California v. Eli Lilly defined the invention by function of the claimed DNA (encoding insulin)].

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species or by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical an/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F. 3d at 1568, 43 USPQ2d at 1406.

The instant claims (especially Claim 14) are drawn to a genus of methods using SCN3A sodium channels (or proteins) that are any amino acid sequences of SEQ ID NO:67, or any protein that is encoded by nucleic acid sequences with at least 95% identity to the sequence of SEQ ID NO:65. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of proteins that are encompassed by the instant claims. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of proteins.

The claimed "SCN3A" sodium channel proteins are not limited to the exact amino acid sequence set forth in SEQ ID NO:67 or to a protein encoded by the exact nucleic acid sequence set forth in SEQ ID No:65. The instant claim recitation (i.e. Claim 14) encompasses any fragments encompassed by the sequence of SEQ ID NO:67, or any amino acid sequence that is encoded by nucleic acid sequences that share at least 95% identity with SEQ ID No:65. The instant specification does not show that any protein fragments encompassed by SEQ ID NO:67 share a common core structure and/or function. For example, a fragment of 10 amino acids of the

N-terminal region may not possess the structure and/or function required by a Sodium ion channel. The instant specification also does not provide representative numbers of species of the various fragments that can possess the required ion channel function and structure.

The nucleic acid sequence of SEQ ID NO:65 has more than 9,000 nucleotides. The instant claimed at least 95% identity would allow a range of at least 90 to 450 nucleotides differences, or 30 to 150 amino acid differences. The instant specification does not provide a common structure and/or function of all mutant proteins that are encoded by nucleic acid sequences share at least 95% identity with SEQ ID NO:65, and the utilization of the mutant proteins in an ion channel assay. The instant specification only provides a few examples of SCN3A mutants (Example 5 of the instant spec.), but no examples of assaying the mutants or wild-type SCN3A sodium channels with various compounds.

In addition, the instant claim 34 is also drawn to a method of selecting a compound that can reduce ion channel activity associated with idiopathic generalized epilepsy (IGE). The instant claim 34 can be broadly interpreted to drawn to a method for selecting a compound that can reduce ion channel activity associated with symptoms of IGE in a patient with IGE. However, the instant specification does not provide any data to correlate the result from the ion channel assay to clinical effectiveness in patients with IGE. In other words, the predictable correlation between in vitro data (i.e. ion channel assay in cells) and in vivo pharmaceutical effects in patients with IGE has not been established.

The art does not teach any sodium channel (such as various mutants of SCN3A) can be used in a screening assay. For examples, Kohling (Epilepsia. Vol. 43 (11): 1278-1295; 2002; cited previously) teaches that there are different types of assays (such as patch clamp) (p. 1281;

p. 1285, right col.), and these assays may or may not produce conclusive results (e.g. "Analysis of spike shape, repetitive firing properties, toxin binding, or sodium uptake only indirectly reflects sodium channel involvements"; p. 1285, right col.). Further, Kohling teaches some drugs have effects on sodium current but at concentrations beyond therapeutic levels, and "thus the mechanism of action cannot be considered to consist of sodium current modulation" (p. 1285, right col.). That is the effects of different drugs (or compounds) on the sodium channel may or may not be conclusive observed by the various type of sodium channel assays. To further illustrate this, the reference reviews various drugs that have been studied (p. 1286+), and from which ESM (p. 1287, right col.) was shown to have different effects on the activity of the sodium channel depending on the how the drug is applied. Valproate was also shown to have "notable" effects on sodium current (produced by sodium channel) only in assays where the drug is internally applied (p. 1289, right col., para 4).

The predictability of suitable assays for monitoring ion channel activity is also discussed in Birch et al (Drug Discovery Today. Vol. 9 (9): 410-418; 2004; cited previously). For examples, the reference teaches the problems associated with various assay methodologies (p. 414, Table 3; p. 415, Table 4). As indicated by the Tables of the reference, there are various factors that can influence the success of a sodium channel assay (such as requirement for high channel expression; Table 3). These effects of these factors are highly unpredictable for different assays as indicated by the reference, and thus rendering the sodium channel assays unpredictable.

Therefore, applicants are not in possession of the genus of assay method using the various proteins, fragments thereof or any mutants thereof of SEQ ID NO:67 or encoded by nucleic acids sharing at least 95% identity with SEQ ID NO:65. Applicants are also not in

possession of methods using ion channel assays to select compounds that would provide in vivo pharmaceutical or therapeutic effects for IGE. Applicant's claimed scope represents only an invitation to experiment regarding possible proteins that can be used with the claimed method.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Discussion and Answer to Argument

11. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the claim amendment has overcome the written description rejection as set forth in the previous office action. (Reply, p.7).

Applicants are respectively directed to the above reformulated written description rejection to address the amended claims.

Scope of Enablement Rejection

12. Claims 14, 34, 36-41, 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assaying sodium channels using protein with full length SCN3A protein of SEQ ID NO:67 or the ion channel encoded by the nucleic acid of

SEQ ID NO:65, as well as a method of selecting a compound using in vitro cell based ion channel assay, does not reasonably provide enablement for using any other protein fragments of SEQ ID NO:67 and/or variants of proteins encoded by SEQ ID NO:65, as well as any assay for selecting a compound that can be used for treating IGE in human or animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection over claims 14-20, 22, 24, 25, 27 and 28 is moot due to applicant's cancellation of the said claims. The rejection over claims 34, 36-41, 43 and 44 is necessitated by applicant's amendment to the claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;
6. The amount of direction or guidance present;
7. The presence or absence of working examples;
8. The quantity of experimentation needed.

The breadth of the claims/The nature of the invention

The instant claims (especially Claim 14) are drawn to a genus of methods using SCN3A sodium channels (or proteins) that are any amino acid sequences of SEQ ID NO:67, or any protein that is encoded by nucleic acid sequences with at least 95% identity to the sequence of SEQ ID NO:65. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of proteins that are encompassed by the instant claims. In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of proteins.

The claimed "SCN3A" sodium channel proteins are not limited to the exact amino acid sequence set forth in SEQ ID NO:67 or to a protein encoded by the exact nucleic acid sequence set forth in SEQ ID No:65. The instant claim recitation (i.e. Claim 14) encompasses any fragments encompassed by the sequence of SEQ ID NO:67, or any amino acid sequence that are encoded by nucleic acid sequences that share at least 95% identity with SEQ ID No:65. The instant specification does not show that any protein fragments encompassed by SEQ ID NO:67 share a common core structure and/or function. For example, a fragment of 10 amino acids of the N-terminal region would not be able to possess the structure and/or function required by a Sodium ion channel. The instant specification also does not provide representative numbers of species of the various fragments that can possess the required ion channel function and structure.

The nucleic acid sequence of SEQ ID NO:65 has more than 9,000 nucleotides. The instant claimed at least 95% identity would allow a range of at least 90 to 450 nucleotides differences. The instant specification does not provide a common structure and/or function of all mutant proteins that are encoded by nucleic acid sequences share at least 95% identity with SEQ ID NO:65, and the mutant protein utilization in an ion channel assay. The instant specification

only provides a few examples of SCN3A mutants (Example 5 of the instant spec.), but no example of assaying the mutants or wild-type SCN3A sodium channels with various compounds.

In addition, the instant claim 34 is also drawn to a method of selecting a compound that can reduce ion channel activity associated with idiopathic generalized epilepsy (IGE). The instant claim 34 can be broadly interpreted to drawn a method for selecting a compound that can reduce ion channel activity associated with symptoms of IGE in a patient with IGE. However, the instant specification does not provide any data to correlate the result from the ion channel assay to clinical effectives in patients with IGE. In other words, the predictable correlation between in vitro data (i.e. ion channel assay in cells) and in vivo pharmaceutical effects in patients with IGE has not been established.

The state of the prior art/ The predictability or lack thereof in the art

The art does not teach any sodium channel (such as various mutants of SCN3A) can be used in a screening assay. For examples, Kohling (Epilepsia. Vol. 43 (11): 1278-1295; 2002; cited previously) teaches that there are different types of assays (such as patch clamp) (p. 1281; p. 1285, right col.), and these assays may or may not produce conclusive results (e.g. "Analysis of spike shape, repetitive firing properties, toxin binding, or sodium uptake only indirectly reflects sodium channel involvements"; p. 1285, right col.). Further, Kohling teaches some drugs have effects on sodium current but at concentrations beyond therapeutic levels, and "thus the mechanism of action cannot be considered to consist of sodium current modulation" (p. 1285, right col.). That is the effects of different drugs (or compounds) on the sodium channel may or may not be conclusive observed by the various type of sodium channel assays. To further

illustrate this, the reference reviews various drugs that have been studied (p. 1286+), and from which ESM (p. 1287, right col.) was shown to have different effects on the activity of the sodium channel depending on the how the drug is applied. Valproate was also shown to have "notable" effects on sodium current (produced by sodium channel) only in assays where the drug is internally applied (p. 1289, right col., para 4).

The predictability of suitable assays for monitoring ion channel activity is also discussed in Birch et al (Drug Discovery Today. Vol. 9 (9): 410-418; 2004; cited previously). For examples, the reference teaches the problems associated with various assay methodologies (p. 414, Table 3; p. 415, Table 4). As indicated by the Tables of the reference, there are various factors that can influence the success of a sodium channel assay (such as requirement for high channel expression; Table 3). These effects of these factors are highly unpredictable for different assays as indicated by the reference, and thus rendering the sodium channel assays unpredictable.

Therefore, applicants are not in possession of the genus of assay method using the various proteins, fragments thereof or any mutants thereof of SEQ ID NO:67 or encoded by nucleic acids sharing at least 95% identity with SEQ ID NO:65. Applicants are also not in possession of methods using ion channel assays to select compounds that would provide in vivo pharmaceutical or therapeutic effects for IGE. Applicant's claimed scope represents only an invitation to experiment regarding possible proteins that can be used with the claimed method.

The level of one of ordinary skill

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction or guidance present/The presence or absence of working examples

The instant specification also does not provide examples of any protein fragments of SEQ ID NO:67, or any protein mutants encoded by nucleic acid sequences share at least 95% identity with SEQ ID NO:65. In addition, the instant specification only provides a few examples of SCN3A mutants (Example 5 of the instant spec.), but no examples of assaying the mutants or wild-type SCN3A sodium channels with various compounds. The instant specification also does not provide any data or example to correlate the result form the ion channel assay to clinical effectives in patients with IGE.

The quantity of experimentation needed

Due to the unpredictabilities of assaying various protein fragments or mutants with various compounds in ion channel assays, undue experimentation would be required. The art has not demonstrated all the possible SCN3A sodium channel variants or protein fragments thereof that can be used in the different assay systems with various compounds. In addition, the art has also not provide general correlation between in vitro cell assay data and in vivo therapeutic effects. Thus, undue experimentation would be required for a person of ordinary skill in the art to use the claimed assay in its full scope.

Conclusion

Therefore based on the evidences as a whole regarding each of the above factors (e.g. factors 1-8), the specification, at the time the application was filed, does not satisfy the enablement requirement for the instant claimed method.

Discussion and Answer to Argument

13. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the claim amendment has overcome the written description rejection as set forth in the previous office action. (Reply, p.8).

Applicants are respectively directed to the above reformulated written description rejection to address the amended claims.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Clare

15. Claims 14, 34, 37-40, 43 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Clare et al (Conference on Molecular and Functional Diversity of Ion Channels and Receptors, New York NY May 14 – 17, 1998, published as Annals of the New York Academy of Sciences. 1999. 868: 80-83; the published article cited in IDS 10/4/06, citation # C76). The previous rejection is maintained for the reasons of record as set forth in the previous Office

action. The rejection over claims 15-20, 22, 24 and 28 is moot due to applicant's cancellation of the said claims. The rejection over claims 37-40, 43 and 44 is necessitated by applicant's amendment to the claims.

The reference cited was published in April 1999, which is before the earliest possible priority date for the instant application (Provisional filing date of 11/26/1999). The citation for the printed article of the Clare reference from PubMed (see attached PubMed citation print out; downloaded 11/14/06) indicates that this is a "Meeting Paper" and that the meeting was held May 14 –17, 1998, which is more than a year before the earliest possible priority date. The meeting included both oral presentations and poster presentations; the enclosed Table of Contents for the printed volume clearly lists the reference by Clare et al. as a "poster paper" (see Table of Contents for Volume 868, p. 2; cited in IDS 10/4/06, citation # C75), as opposed to an oral presentation. The reference thus qualifies as a "printed publication" within the meaning of 35 USC 102(b); see MPEP § 2128.01(IV).

The instant claims recite a method for selecting a compound which reduces an activity of a SCN3A sodium channel comprising:

(a) contacting a composition comprising a SCN3A sodium ion channel protein with a test compound;

(b) assaying the activity of the sodium ion channel in the presence of the test compound;

(c) comparing the activity of the sodium ion channel in the absence of said test compound;

(d) selecting a compound which reduces the activity of the sodium ion channel as compared to the activity of the sodium ion channel in the absence of the test compound; wherein said SCN3A protein is selected from the group consisting of (i) an amino acid sequence set forth in SEQ ID NO:67; and (ii) a SCN3A protein expressed by a SCN3A nucleic acid sequence having at least 95% identity to the nucleic acid sequence as set forth in SEQ ID NO:65.

Clare et al, throughout the publication, teach cloning and functional analysis of the Type III sodium channel from human (p. 80, para 1-2), which the Type III sodium channel reads on the SCN3A sodium channel (both the nucleic acid sequence and the protein) of **clm 14**.

The reference teaches assaying the ion channel by using tetrodotoxin (TTX) (p. 80, para 3; p. 81, Figure 1), which the TTX reads on "a compound" of **clm 14**.

The reference also teaches measuring the inhibition of the sodium channel activity using TTX and compared to controls (p. 81, Figure 1), which reads on steps (a)-(d) of **clm 14** as well as the method of **clm 43**. This also reads on the difference observed between the inactivation (or activity) of the sodium channel in the presence and absence (e.g. Control and Wash of Figure 1, top panel) of a test agent, as recited in **clm 14**, as well as the property of reducing ion channel activity of **clm 34**.

Although the reference does not explicitly teach the specific nucleic acid sequence (as recited in **clm 14**: SEQ ID No 65) or the protein sequence (as recited in **clms 14** and **44**: SEQ ID No 67) of the SCN3A (or Type III) sodium channel, the specific nucleic acid and amino acid sequences are inherent properties of the human Type III (SCN3A) sodium channel. The reference teaches cloning the Type III sodium channel into a vector and expressing the channel

in host cells (p. 80, para 3), which cloning and expression steps would require the nucleic acid sequence that encode for and the amino acid sequence of the SCN3A ion channel. The reference also teaches that the Type III sodium channel is from human adult (p. 80, para 2), and the mRNA having the nucleic acid sequence for the SCN3A gene (p.83, para 3).

In addition, the instant specification discloses that SEQ ID NO 65 is the cDNA sequence of the human adult form SCN3A (p. 27, line 24 and Sequence Listing of the instant spec.), and SEQ ID No 67 is the protein sequence of the human adult form of SCN3A (p. 27, line 26 and Sequence Listing of the instant spec.). The instant specification also discloses that the SCN3A is found in the brain (p. 5-6, bridging para), which is the source of the SCN3A nucleic acid of the reference (p. 80, top of para 2). The human type III ion channel α subunit (or SCN3A) of the reference appears to have the same nucleic acid or amino acid sequences as the ones represented by SEQ ID Nos 65 and 67 of the instant application, because the gene and protein sequences for type III ion channel α subunit would not be different regardless what the gene or the protein is named.

The reference teaches cloning the Type III sodium channel into a vector and expressing the channel in host cells (p. 80, para 3), which read on the cloning and expression steps of **clms 37** and **38**.

The reference also teaches measuring the ion channel activity in the transfected HEK293T cells (e.g. p.80, para 3), which reads on the assay step of **clm 39**.

The reference also teaches voltage dependent activation (e.g. pp.80-81), which reads on the ion channel activity of **clm 40**.

Discussion and Answer to Argument

16. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants state "Applicants do not agree with the Examiner's allegation that Clare et al., is a "Meeting Paper... held 14-17 May 1998". (Reply, 3/28/07, p.9, para 2).

However, applicants made the above statement without further elaboration as to why the Clare reference cannot be considered a "meeting paper".

Applicants argue the Clare reference does not "inherently" teach the specific SEQ ID Nos: 65 and 67, as recited in the instant claims. (Reply, 3/28/07, pp.9-10).

Applicants argue "for a reference to anticipate based on inherency, the inherency must be '**certain**'." (emphasis in original). Applicant cites In re Oelrich and Ex parte Cyba in support of this argument. While the cases cited do state that what is asserted to be inherent must necessarily be present, several other cases as well as MPEP § 2112, support the examiner's contention that the burden is on applicant to distinguish what is now claimed from the product disclosed in the prior art. See for example *In re Best* 195 USPQ 430, 433 (CCPA 1977), where the court stated:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, 4 the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Here, the product disclosed in the prior art is a nucleic acid that encodes a type III sodium channel and is isolated from human brain (see Clare, title). Instant SEQ ID NO:65 is "the cDNA sequence of the adult form of SCN3a" (specification, p. 27, lines 24 – 25). "SCNA" means sodium channel (specification, p. 3 lines 18 – 19). The only difference between "SCN3A" as defined in the specification and "Type III Na+ channel" as referred to by Clare appears to be the choice of Arabic numbers in the former and Roman numerals in the latter. Both are type 3 (or III) sodium channels, both are from humans. Thus as in Best, the product now claimed appears to be identical to that in the prior art. Because the PTO cannot manufacture and compare the prior art product and applicant's claimed invention, the burden is on applicant to distinguish the claimed invention from the prior art product.

MPEP § 2112 IV states a scientific rationale tending to show inherency must be provided. In the previous Office action as well as the discussion above, a scientific rationale was provided to show inherency. The reference by Clare provides evidence that the product encodes a type III sodium ion channel α subunit; see for example Clare, Figure 1 which shows the channel is voltage dependent and tetrodotoxin (TTX) sensitive. The Clare reference also teaches the nucleic acid (encoding for the type III sodium ion channel α subunit) is reported to be about 9.5 kb in size, as indicated by the Northern blot (Clare, Figure 2); note the nucleic acid is isolated on the blot and the ~ character in front of 9.5 kb indicates it is an approximate size. Applicant's SEQ ID NO:65 is 9112 nucleotides, or 9.1 kb. Thus the nucleic acid of the Clare reference encoding for the Type III ion channel α subunit appears to be the same as the nucleic acid of SEQ ID NO:65 of the instant claims. That is they have the same name, they were isolated from the same tissue, are approximately the same size, and both encode sodium channels.

Alternatively, the prior art product comprises instant SEQ ID NO:65, as the prior art may be slightly larger (~9.5 kb vs. 9.1 kb)

MPEP § 2112 V states that "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference" (see heading). Applicant argues that the product now claimed is different from that in Clare.

In support of the argument, applicant sets forth the following evidence:

1) Clare detects two bands, one being ~9.5 kb and the other being ~7.5 kb. The 7.5 kb band is present in skeletal muscle, whereas SCN3A from Thimmapaya et al. (2005) is not present in skeletal muscle

2) The probe from Clare detects another nucleic acid, which applicant speculates may be SCN4A.

3) The $V_{1/2}$ for the channel encoded by Clare's nucleic acid is 58 mV, whereas the $V_{1/2}$ for SCN3A from Chen et al. (2000) is slightly higher (69 mV).

Each of the above points will be addressed in turn.

With respect to 1), whether or not the probe used by Clare either detects multiple bands or detects a product in skeletal muscle is not germane. The product at 9.5 kb, which is highly expressed in brain and isolated on the Northern blot, is the one that is patently indistinguishable from the nucleic acid of SEQ ID NO:65. Although the probe used by Clare does in fact detect more than one band, the probe is not identical to the cDNA that encodes the type III sodium channel. In fact, Clare et al. are careful to point out that the entire cDNA was not used as a

probe; only a portion from the 5' untranslated region was used (p. 83, first complete paragraph). The smaller (7.5 kb) band is hypothesized to be a splice variant but whether or not it is such a variant is immaterial as to the identity of the full-length cDNA which encodes a functional sodium channel or of the 9.5 kb band.

With respect to 2), as was stated in the previous paragraph, whether or not the probe detects an additional nucleic acid is not relevant. The probe is not the full-length cDNA. It is from the 5' UTR (see Clare p. 83). The full-length cDNA, which encodes a functional sodium channel and the 9.5 kb band isolated on the Northern blot are both indistinguishable from the nucleic acid now claimed. Thus even if the 7.5 kb band is SCN4A as applicant argues, the prior art reference by Clare still anticipates the claimed invention.

With respect to 3), the differences appear to be slight (58 vs 69 mV) and may be the result of re-calculation of data. Note that the data depicted as Figure 1 in Clare et al. appear to be identical to those set forth in Figure 5 of Chen (2000. European Journal of Neuroscience 12:4281-4289, cited in remarks filed 29 January 2007. Note that in each case the error bars are small between –120mV and –80 mV, are relatively large from –60mV to –40mV, and are small again at –10mV. Further in each case n=4 (see figure legends). The data appear to be the same, only the calculations differ. Thus is applicant is attempting to show that the data depicted in Chen (2000) are the true SCN3A data differences from those results are evidence of a different protein encoded by a different nucleic acid, the data are not convincing.

It is noted that applicants have attempted to distinguish the prior art product from Clare from those disclosed in Chen and in Thimmapaya, but have not provided evidence to distinguish the nucleic acid now claimed from Clare.

For the reasons above and previously made of record, the rejection over Clare is maintained.

New Claim Rejections

Claim Rejections - 35 USC § 112

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

18. Claims 14, 34, 36-41, 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 has been amended to recite "a SCN3A nucleic acid sequence having at least 95% identity to the nucleic acid sequence as set of forth in SEQ ID NO:65" as filed on 3/28/07. However, the instant specification does not provide support for the claimed range of nucleic acid sequences that have at least 95% identity to SEQ ID NO:65.

Claim 34 has been added as part of the claim amendment filed on 3/28/07. However, the instant specification does not provide support for the claimed "a human SCN3A protein associated with idiopathic generalized epilepsy (IGE)".

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 14 and its dependent claims (encompassing all limitations of the said independent claim) as well as claim 34 represent new matter.

Second paragraph of 35 U.S.C. 112

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 36 recites "wherein the test compound is a library of test compounds", which is unclear. The phrase "the test compound" is in the singular form, which has antecedent basis in Claim 14 that also recite the "test compound" in the singular form (i.e. "a test compound"). It is not clear how a single "test compound" can be "a library of test compounds" (i.e. a plurality of compounds).

Claim Rejections - 35 USC § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Clare and Hall

22. Claims 14, 34, 36-40, 41, 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clare et al (Conference on Molecular and Functional Diversity of Ion Channels and Receptors, New York NY May 14 – 17, 1998, published as Annals of the New York Academy of Sciences. 1999. 868: 80-83; the published article cited in IDS 10/4/06, citation # C76), in view of Hall et al (US 5,871,940; 2/16/1999; filed 1/13/1997). This rejection is necessitated by applicants' amendment to the claims.

Clare et al, throughout the publication, teach cloning and functional analysis of the Type III sodium channel from human by incubation with a compound, as discussed supra.

Clare et al do not explicitly teach screening a library of compounds as recited in **clm 36**, and using techniques such as two electrode voltage clamp as recited in **clm 41**.

However, Hall et al, throughout the patent, teach using ion channels to screen for "compounds" or "agents" (e.g. Claim 1; col.3, lines 15+; col.4, lines 1+). The reference also teaches using patch clamp (e.g. col.2, line 8) and two-microelectrode voltage clamp (col.25, lines 40+) to measure Na ion channel activity.

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to screen a library of compounds (i.e. a plurality of compounds) using ion channel assays measured by patch clamp or two electrode voltage clamp techniques.

A person of ordinary skill in the art would have been motivated at the time of the invention to screen a library of compounds (i.e. a plurality of compounds), because screening a library of compounds would offer the advantages of identifying compounds for useful

applications such as insecticides and therapeutic agents as taught by Hall et al (e.g. col.3, lines 11+).

A person of ordinary skill in the art would have been motivated at the time of the invention to measure ion channel activities using patch clamp or two electrode voltage clamp techniques, because the said techniques are routine and known in the art for measuring ion channel activities as taught by Hall et al.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since Clare et al and Hall et al have demonstrated the success of measuring the effect of various compounds on Sodium ion channel activity using various techniques such as voltage clamp assays.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
9/26/07

/Jon D. Epperson/
Primary Examiner, AU 1639